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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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JONES DAY
222 EAST 41ST ST
NEW YORK, NY 10017

EXAMINER	
YU, MISOOK	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 02/10/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/724,406	FRANCISCO ET AL.	
	Examiner	Art Unit	
	MISOOK YU, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 November 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,11,13-19 and 67* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,11,13-19 and 67* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7/15/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7/15/2004, and 11/05/2004 including Dr.Klussman's declaration has been entered.

Claim 67 is amended. Claims 1-8, 11, 13-19, and 67 are pending, and examined on merits.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

This Office action contains new grounds of rejection.

Claim Rejections - 35 USC § 112, Withdrawn

The rejection of claim 67 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is **withdrawn** in view of the amendment.

The rejection of Claim 67 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is also **withdrawn** in view of the amendment.

Claim Rejections - 35 USC § 102, Withdrawn

The rejection of claims under 35 U.S.C. 102(b) as being anticipated by WO 96/22384 (25 July 1996) is withdrawn for the following reasons. Applicant argument that WO 96/22384 is mostly about newly generated anti-CD 30 antibodies, and upon review and reconsideration of the art, the Office could not meet the burden that WO 96/22384 explicitly or implicitly teaches a method of treating Hodgkin's disease using HeFi-1 or C10, although HeFi-1 and C10 are disclosed in WO 96/22384.

Claim Rejections - 35 USC § 103, Withdrawn

The rejection of claims under 35 U.S.C. 103(a) as being unpatentable over WO 96/22384 as applied to claims 1-5, 7, 8, 11, 13, 15, 16, and 19 above, and further in view of Barth et al (June 2000, Blood, vol. 95, page 3909-14) is withdrawn because the Office considers that WO 96/22384 is no longer art as explained above.

Double Patenting, Withdrawn

The provisional double patenting due to duplicate claims is withdrawn in view of amendment.

The Following Are New Grounds of Rejection

Specification

The disclosure is objected to because it, for example at page 30 line 26 contains an embedded hyperlink and/or other form of browser-executable code. Applicant is kindly requested to go over the entire specification very carefully to see other embedded hyperlinks and/or other form of browser-executable codes in the specification. Applicant

is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 8, and 13-19 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for in vivo tested antibodies of Pohl et al., of record (see below), does not reasonably provide enablement for any other anti-CD antibodies for the method of treating Hodgkin's disease. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use and make the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

Claim 8 recites specific cell lines of "HeFi-1" or "AC10".

It is apparent that the recited cell lines are required to practice the claimed invention in claim 8, and also for the claimed invention in the dependent claims 13-19

because they are specifically required in the claims. As required elements they must be known and readily available to the public or obtainable by a repeatable method set forth in the specification, or otherwise readily available to the public. If it is not so obtainable or available, the enablement requirements of 35 U.S.C. § 112, first paragraph, may be satisfied by a deposit of the cell lines listed in claim 7. See 37 CFR 1.802.

The specification does not provide a repeatable method for obtaining the cell lines of claim 8, and nor do they appear to be readily available material. Deposit of the cell lines would satisfy the enablement requirements of 35 U.S.C. 112. While the specification states on page 5 that the cell lines "have been deposited for patent purposes", the specification does not indicate the terms of the deposit.

If a deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made under the terms of the Budapest Treaty and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. See 37 CFR 1.808.

If a deposit is not made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made at an acceptable depository and that the following criteria have been met:

(a) during the pendency of this application, access to the invention will be afforded to one determined by the Commissioner to be entitled thereto;

(b) all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon granting of the patent;

(c) the deposit will be maintained for a term of at least thirty (30) years and at least five (5) years after the most recent request for the furnishing of a sample of the deposited material;

(d) a viability statement in accordance with the provisions of 37 CFR 1.807; and

(e) the deposit will be replaced should it become necessary due to inviability, contamination or loss of capability to function in the manner described in the specification.

In addition the identifying information set forth in 37 CFR 1.809(d) should be added to the specification. See 37 CFR 1.803 - 37 CFR 1.809 for additional explanation of these requirements.

Amendment of the specification to recite the date of deposit and the complete name and address of the depository is required. As an additional means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

If a deposit is made after the effective filing date of the application for patent in the United States, a verified statement is required from a person in a position to corroborate that the biological material described in the specification as filed is the same

as that deposited in the depository, stating that the deposited material is identical to the biological material described in the specification and was in the applicant's possession at the time the application was filed.

Applicant's attention is directed to In re Lundak, 773 F.2d. 1216, 227 USPQ 90 (CAFC 1985) and 37 CFR 1.801-1.809 for further information concerning deposit practice.

Claim Rejections - 35 USC § 103

Claims 1, 2, 5, 7-13, 16, 19, and 67 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pohl et al., of record (1993, Int. J. Cancer, vol. 54, pages 418-425).

The claims are interpreted as drawn to method of Hodgkin's disease treatment by administering an anti-CD 30 antibody that exerts cytotoxic effect on Hodgkin's disease cell lines in the absence of conjugation to cytotoxic agent, wherein said antibody in claim 2, 5, 13, 16 is recombinant, wherein claims 7, 19, and 67 specify how the cytotoxic effect is determined, wherein claim 8 specifies said antibody competes with HeFi-1 and AC10 for binding to CD30 antigen, and wherein the antibody in claim 11 comprises a protein comprises at least 95 % identity to instant SEQ ID NO:2.

Pohl et al., teach: (1) Hodgkin's disease treatment art has been facing with problem due to "a high rate of relapse", and suggest an active immunotherapy to solve the high rate of relapse using an antibody binding to CD30 by administering an anti-CD 30 antibody binding CD30 expressed in of Hodgkin's disease (note 1st paragraph); (2) "murine monoclonal ab2β 9G10, 14G9 induced a CD30 specific T- and B –cell

response" in vivo at page 418, left column, 1st paragraph; (3) AB3 4A4 antibody at Figs. 7-10 that exerts cytotoxic effect on Hodgkin's disease cell lines in the absence of conjugation to cytotoxic agent, and prevent tumor-cell growth in vivo model.

Therefore, it would have been obvious to use ab2β 9G10, 14G9, AB3 4A4 for treating patient with Hodgkin's disease, especially when the tumor burden is low after the initial chemotherapy to prevent relapse, given Pohl et al., suggesting phase-1 clinical human trial for Hodgkin lymphoma at the last line at page 425. This would have been accomplished with a reasonable expectation of success given in vivo study is already done using the in vivo model as shown at Fig. 10.

As for the specific method of determining the cytotoxic effect as disclosed in instant claims 7, 19, and 67, or the antibody competing with HeFi-1 and AC10 for binding to CD30 antigen as in the instant claim 8, the Office does not have the facilities and resources to provide the factual evidence needed in order to establish that ab2β 9G10, 14G9, or AB3 4A4 of Pohl et al., do not possess the cytotoxic effect if the cytotoxicity is determined by the method in the instant claims 7, 19, and 67 instead of the method disclosed at the paragraph bridging right and left columns at page 420 of Pohl et al. The Office cannot test whether the antibody competes with binding HeFi-1 and AC10.

As for at least 95 % identity to instant SEQ ID NO:2 in the instant claim 11, as discussed during the prosecution history, for example, \ in the Office action mailed on 04/03/2003, any murine antibody inherently comprises a protein comprising at least 95 % identity to instant SEQ ID NO:2. Note the previously provided sequence alignment

(with the Office action mailed on 04/03/2003) that the instant SEQ ID NO:2 has about 98 % sequence identity to any mouse immunoglobulins light chain. Thus, murine monoclonal ab2β 9G10, 14G9 that induce a CD30 specific T- and B –cell responses, are same product as instant claimed product in the instant claim 11, and murine monoclonal ab2β 9G10, 14G9 binds to CD30.

It appears that **the product**, i.e. an anti-CD30 antibody being used in the instant claims and in the method of Pohl et al., (1993), appears to be the same. In the absence of evidence to the contrary, the burden is on the applicant to prove that the product being used in the claimed method is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

As for claim 2, 5, 13, 16, Pohl et al., (1993) at page 419, left column, 1st paragraph teach that making a recombinant antibody is well known before the effective filing date of the instant application. Therefore, it would have been obvious to make and use recombinantly made ab2β 9G10, 14G9, AB3 4A4 for treating patient with Hodgkin's disease, given Pohl et al., suggesting phase-1 clinical human for Hodgkin lymphoma at the last line at page 425.

Claims 1, 3, 8, 11, 14, 16, 18, are rejected under **35 U.S.C. 103(a)** as being unpatentable over Pohl et al., (cited above), and further in view of Barth et al., of record (June 2000, Blood, vol. 95, page 3909-14).

The claims are interpreted as drawn to method of Hodgkin's disease treatment by administering anti-CD 30 antibody in combination with other known conventional chemotherapy.

Pohl et al., teach method of inducing an good immune response using an anti-CD30 antibody that could be used to kill residual tumor after "combined modality treatment" (note 1st sentence at page 418) that could include chemotherapy.

Pohl et al., do not specifically say "chemotherapy".

However, Barth et al., teach that conventional chemotherapy works quite well in treating Hodgkin's disease and further teach that anti-CD30 antibody might be useful for killing the residual tumor cells that escapes from the conventional chemotherapy and causes relapse later. Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to use anti-CD30 antibody to kill residual tumor cells to prevent relapse after the chemotherapy.

Claims 1, 4, 6, 8, 11, 15, 17 are rejected **under 35 U.S.C. 103(a)** as being unpatentable over Pohl et al., (cited above), in view of Barth et al (June 2000, Blood, vol. 95, page 3909-14), and further in view of da Costa et al., of record, 2000, Cancer Chemother Pharmacot, 46(suppl):S33-S36.

The claims are interpreted as drawn to method of Hodgkin's disease treatment by administering the anti-CD 30 antibody of the respective base claims conjugated to cytotoxic agent or the conjugated antibody in combination with other known conventional chemotherapy.

Pohl et al., teach method of inducing an good immune response using an anti-CD30 antibody that could be used to kill residual tumor after conventional other "combined modality treatment" (note 1st sentence at page 418) that could include chemotherapy.

Barth et al., teach that conventional chemotherapy works quite well in treating Hodgkin's disease and further teach that anti-CD30 antibody might be useful for killing the residual tumor cells that escapes from the conventional chemotherapy and causes relapse later.

Neither Pohl et al., nor Barth et al., teach an anti-CD 30 antibody of the respective base claims conjugated to cytotoxic agent.

However, da Costa et al., teach an anti-CD 30 antibody conjugated to cytotoxic agent, for example alpha CD3/CD30 antibody (note abstract) that used in Hodgkin's disease treatment.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to conjugate the various useful cytotoxic agents to CD30 antibody of Pohl et al., for Hodgkin's disease treatment in combination with chemotherapy to kill residual tumor cells to prevent relapse after the chemotherapy.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MISOOK YU, Ph.D. whose telephone number is 571-272-0839. The examiner can normally be reached on 8 A.M. to 5:30 P.M., every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MISOOK YU, Ph.D.
Examiner
Art Unit 1642

JEFFREY SIEW
SUPERVISORY PATENT EXAMINER
2/7/05